UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/399,120	09/20/1999	DESMOND MASCARENHAS	220952029300	1886

7590 02/23/2007

Ms. Beth Burrous
Foley & Lardner
Washington Harbour
3000 K Street N W Suite 500
Washington, DC 20007-5109

EXAMINER	
GUPTA, ANISH	
ART UNIT	**PAPER NUMBER**
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/399,120	MASCARENHAS, DESMOND	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,16 and 18-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-10,16,18-21,23-44 and 47-50* is/are allowed.

6)☒ Claim(s) *22,45 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants amendment, filed November 22, 2006 is acknowledged. Applicants amended the specification, paragraph [005].

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 22, 45, 46 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of slowing or treating cancer using an effective amount of null insulin-like growth factor I (null-IGF-I). The claims in question recite specific null-IGF-I that have alterations of residues 28-37 replaced with four glycine residues (claim 22), and specifically mutated IGF molecules as recited in claims 45-46.

Lack of *Ipsis Verbis* Support

The specification is void of any literal support for the specific IGF molecules claimed. The specification, on page 10, provides support for the null IGF molecule Y60L, where the 60th residue of the IGF molecule has been replaced by Leucine. However, the specification does not provide any literal support for other Null IGF-1 molecules claimed such as [Ala-31, Leu-60 IGF-I], [Leu24,

Leu 60, IGF-1], [Leu24, Ala31, Leu60] IGF-I, [1-27, Gly4, 38-70]; [Ser24]IGF-1, and [Leu24, 1-62]IGF-1, and any IGF molecule where residues 28-37 have been replaced with four glycine residues.

Lack of Implicit or Inherent Support

"While there is no in *haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure." See MPEP 2163. Thus, support can be furnished implicitly or inherently for a specifically claimed limitation. However the specification lack any implicit or inherent support for the claimed IGF molecules. On page 5, which defines Null IGF, the specification states that Null-IGF include "variants in which one or more which one or more of IGF-I's tyrosine residues (i.e., residues 24, 31, or 60) are replaced with non-aromatic residues (i.e, other than tyrosine, phenylalsnine or tryptophan), variants where amino acid residues 49, 50, 51, 53, 55 and 56 are altered (for example, where residues 49-50 are altered to Thr-ser- Ile or where residues 55-56 are altered to Tyr-G1n), and combinations thereof." The specification fails to provide any support that "non-aromatic" amino acids specifically include Serine, providing support for [Ser24]IGF-1. In the context of non aromatic amino acids, the specification only provides support for the substitution of leucine in position 60. Further, the definitions do not lead one to conclude that truncated analogs such as [Leu24, 1-62]IGF-1 and analogs with four glycine residues are within the meaning of the Null IGF definition.

In a telephone interview, Applicants stated that support for the specific analogs could be found in the reference of Cascieri et al. (1988 and 1989), Bayne et al. (1990), and Baxter et al. (1992), cited on page 5 of the specification and which are incorporated by reference into the disclosure. However, this does not provide support for the specific IGF-1 molecules for two reasons.

First, 37 CFR 1.57(c) prohibits incorporation by reference to essential subject matter using non-patent literature. 37 CFR 1.57(c) recites:

> (c) " **Essential material** " may be incorporated by reference, but **only by way of an incorporation by reference to a U.S. patent or U.S. patent application publication**, which patent or patent application publication does not itself incorporate such essential material by reference. "Essential material " is material that is necessary to:
> (1) Provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112;
> (2) Describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112; or
> (3) Describe the structure, material, or acts that correspond to a claimed means or step f or performing a specified function as required by the sixth paragraph of 35 U.S.C. 112."

The claimed subject matter is "Essential material" since it provide it provides written description as defined in sub paragraph (1). Since the "Essential material," claimed in the instant application, is not recited in a "U.S. patent or U.S. patent application publication, which patent or patent application publication does not itself incorporate such essential material by reference," it is improper to provide support via the "incorporation by reference" means.

Secondly the decision of Ex Parte Raible, 8 USPQ2d 1709 (BPAI) is controlling in this case. In Raible, Appellants attempted to use the doctrine of incorporation by reference to provide support for a claimed limitation. The Board stated the doctrine of incorporation by reference could not be used by Appellant since the specification did not contain a specific indication of the features disclosed by the incorporating reference which corresponded to the features specifically claimed. See Raible at 1710. Further the specification did not "identify the specific portions of the patent which appellant may have intended to rely upon to supplement his disclosure." Raible at 1710. The Board concluded "[t]he purpose of incorporation by reference in an application of matter elsewhere

written down is for economy, amplification, or clarity of exposition, by means of an *incorporating statement clearly identifying the subject matter which is incorporated and where it is to be found."* Raible at 1710.

Here, the instant specification fails to provide "an incorporating statement clearly identify the subject which is corporate and where it is to be found." Bayne reference recites teaches seven IGF analogs that have point mutation at positions 24, 31, 60, multiple mutations at 24, 31, and 60 that meet the definition of Null IGF, Cascieri et al. (1989) disclose one IGF molecules that falls within the claimed definition, Baxter (1992) discloses numerous analogs, such as [Tyr 15, Leu16] IGF-I, [Gln3, Ala4, Tyr15, Leu16] IGF-1, [Ser24 IGF I], [1-62 IGF 1], [Leu 24, 1-62] IG-1, [Tyr 55, Gln 56] IGF-1, [1-27, Gly4, 38-70] IGF-1, [1-27, Gly4, 38-62] IGF-1, that fall within Applicants definition of IGF, and Cascieri (1988) teahes three IGF molecules . Of these, only few have been claimed in the instant application. The instant specification does not provide any "statement clearly identify" that the specifically claimed IGF analogs fall within the definition of the claimed invention and are incorporated by reference. Hence, it cannot be said that the reference cited provide implicit or inherent support.

Response to Arguments

Applicants state that paragraph [0034] recites that the "[t]he patents, patent applications, and publications cited throughout the disclosure are incorporated herein by reference in their entirety." Accordingly, the references Cascieri, Bayne and Baxter references referred to in paragraph [005] provide written description for the null IGF's claimed in claims 22, 45, 46.

Further, Applicants state that information incorporated by reference does not fall within the definition of "essential material" provided by the C.F.R. The claimed invention is directed to methods of slowing the growth rate of a tumor or slowing progression of cancer comprising administration of uncomplexed null IGF-I. "The present invention, however, is not based on the

discovery of new null IGF compounds. Therefore, the material incorporated by reference relates to specific null IGFs already known in the art and the application specifically indicates that the IGF-I variants in the Cascieri, Bayne and Baxter references are suitable for use in the present invention.

Applicant's arguments have been fully considered but have not been found persuasive.

Unlike Applicants contentions, the subject matter in issue of claims 22, 45, and 46, is required to practice the claimed invention. The claims require that specific null IGF-I molecules be utilized to slow the growth rate of a tumor or slow progression of cancer and therefore are necessary to practice the claimed invention. Thus, the null IGF-I, which is altered such that residues 28-37 are replaced with four glycine residues, and null IGF-I, [Leu 60] IGF-I, [Ala31, Leu60] IGF-I; [Leu24, Leu60] IGF-I; [Leu24, Ala31, Leu60] IGF-I; [1-27, Gly4, 38-70] IGF-I; [Ser24] IGF-I; and [Leu24, 1-62} IGF-I are necessary to provide a written description of the claimed invention, as required by the first paragraph of 35 U.S.C. 112.

Applicants state that material incorporated by reference relates to specific null IGFs already known in the art and the application specifically indicates that the IGF-I variants in the Cascieri, Bayne and Baxter references are suitable for use in the present invention. However, as stated in the previous office action, the specification did not "identify the specific portions of the patent which appellant may have intended to rely upon to supplement his disclosure." Raible at 1710. In Riable, the Board concluded "[t]he purpose of incorporation by reference in an application of matter elsewhere written down is for economy, amplification, or clarity of exposition, by means of an *incorporating statement clearly identifying the subject matter which is incorporated and where it is to be found."* Raible at 1710. The instant specification fails to provide "an incorporating statement clearly identify the subject which is corporate and where it is to be found," because of the null IGF molecules disclosedin Cascieri, Bayne and Baxter, only a few have been claimed in the instant application.

Applicants have failed to address how the incorporating statements clearly identifying the subject matter which is incorporated and where it is to be found.

Rejection is maintained.

New Grounds For Rejections

Specification

3. The amendment filed 11-22-06 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

Applicants have amended the specification to recite specific Null IGF-1 molecules disclosed in the reference of Cascieri et al., Bayne et al. and Baxter et al. Specifically, the amendment added the Null IGF-1 molecule [Ser24] IGF-I as being taught by Cascieri et al., Ala31, Leu60] IGF-I, [Leu24, Leu60] IGF-I, and [Leu24, Ala31, Leu60] IGF-I as being taught by Bayne et al. and IGF-I, and [Leu24, 1-62] IGF-I as being taught by Baxter et al.

The original disclosure did not contain any disclosure of specific Null IGF molecules taught by the three references. The specification only stated that "[d]escriptions of null IGF-I's may be found in Cascieri et al. (1988) Biochemistry 27:3229-3233; (1989) J.. Biol. Chem. 264:2199-2202), Bayne et al. (1990) J. Biol. Chem. 265:15648-15652) and Baxter et al. (1992) J. Biol. Chem. 267:60-65)" (see page 5 of the original disclosure). While the specification did state "[t]he patents, patent application, and publication cited throughout the disclosure are incorporated herein by reference in their entirety," this does not provide ample support for the amendment for the following reasons.

37 CFR 1.57(c) prohibits incorporation by reference to essential subject matter using non-patent literature. 37 CFR 1.57(c) recites:

> (c) " **Essential material** " may be incorporated by reference, but **only by way of an incorporation by reference to a U.S. patent or U.S. patent application publication,** which patent or patent application publication does not itself incorporate such essential material by reference. "Essential material " is material that is necessary to:
> (1) Provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112;
> (2) Describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112; or
> (3) Describe the structure, material, or acts that correspond to a claimed means or step f or performing a specified function as required by the sixth paragraph of 35 U.S.C. 112."

The claimed subject matter is "Essential material" since it provide it provides written description as defined in sub paragraph (1). Since the "Essential material," claimed in the instant application, is not recited in a "U.S. patent or U.S. patent application publication, which patent or patent application publication does not itself incorporate such essential material by reference," it is improper to provide support via the "incorporation by reference" means.

The decision of Ex Parte Raible, 8 USPQ2d 1709 (BPAI) is controlling in this case. In Raible, Appellants attempted to use the doctrine of incorporation by reference to provide support for a claimed limitation. The Board stated the doctrine of incorporation by reference could not be used by Appellant since the specification did not contain a specific indication of the features disclosed by the incorporating reference which corresponded to the features specifically claimed. See Raible at 1710. Further the specification did not "identify the specific portions of the patent which appellant may have intended to rely upon to supplement his disclosure." Raible at 1710. The Board concluded "[t]he purpose of incorporation by reference in an application of matter elsewhere written down is for economy, amplification, or clarity of exposition, by means of an *incorporating statement clearly identifying the subject matter which is incorporated and where it is to be found."* Raible at 1710.

Here, the instant specification fails to provide "an incorporating statement clearly identify the subject which is corporate and where it is to be found." Bayne reference recites teaches seven IGF analogs that have point mutation at positions 24, 31, 60, multiple mutations at 24, 31, and 60 that meet the definition of Null IGF, Cascieri et al. (1989) disclose one IGF molecules that falls within the claimed definition, Baxter (1992) discloses numerous analogs, such as [Tyr 15, Leu16] IGF-I, [Gln3, Ala4, Tyr15, Leu16] IGF-1, [Ser24 IGF I], [1-62 IGF 1], [Leu 24, 1-62] IG-1, [Tyr 55, Gln 56] IGF-1, [1-27, Gly4, 38-70] IGF-1, [1-27, Gly4, 38-62] IGF-1, that fall within Applicants definition of IGF, and Cascieri (1988) teahes three IGF molecules . Of these, only few have been claimed in the instant application. The instant specification does not provide any "statement clearly identify" that the specifically claimed IGF analogs fall within the definition of the claimed invention and are incorporated by reference. Hence, it cannot be said that the references cited provided the required support.

Applicant is required to cancel the new matter in the reply to this Office Action.

Allowable Subject Matter

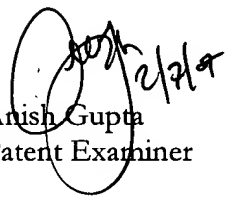
4. Claims 1-10, 16, 18-21, 23-44, 47-50 are allowed.

5. Applicant's amendment to the specification necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the

THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (571) 272-0562. The fax phone number of this group is (571)-273-8300.



Anish Gupta
Patent Examiner